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CASE REPORT

Reversible myocardial oedema due to acute myocardial infarction as differential diagnosis of cardiac transthyretin amyloidosis

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Abstract

Using bone-avid radiotracers, cardiac transthyretin (TTR) amyloidosis can be diagnosed by scintigraphy, thus obviating endomyocardial biopsy. Radiotracer accumulation, however, may also be due to other causes. A 68-year-old male with acute myocardial infarction underwent recanalization of the left anterior descending coronary artery (LAD). Postinterventionally, transthoracic echocardiography showed hypokinesia of the septum and anterior wall and a thickened myocardium with granular sparkling appearance. Cardiac amyloidosis was suspected. A 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid whole-body scan 4 days after LAD recanalization showed Perugini 2 myocardial tracer uptake. Monoclonal gammopathy was excluded, and cardiac TTR amyloidosis was diagnosed. Three months later, 99m-Tc-hydroxydiphosphate scan showed no myocardial tracer uptake. Cardiac magnetic resonance imaging revealed late gadolinium enhancement within the LAD supply area. No mutation of the *TTR* gene was found. Suspicion of amyloidosis should consider not only echocardiography but also history and clinical findings. Myocardial oedema due to reperfusion should be acknowledged as a differential diagnosis for cardiac uptake of bone-avid radiotracers.

Keywords Bone scintigraphy; Myocardial infarction; Echocardiography; Cardiac magnetic resonance imaging; Transthyretin amyloidosis

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Introduction

Cardiac amyloidosis resulting from myocardial deposition of misfolded transthyretin (TTR) is increasingly gaining attention due to advances in imaging and medical treatment.[1,2] Radionuclide imaging with bone-avid radiotracers is reported to specifically detect TTR cardiac amyloidosis, thus obviating the need for endomyocardial biopsy to establish the diagnosis.[1,3,4] The 2017 consensus document of the European Association of Cardiovascular Imaging (EACVI) and the Working Group on myocardial and pericardial diseases of the European Society of Cardiology (ESC) on multimodality imaging in restrictive cardiomyopathy states that the diagnosis of cardiac TTR amyloidosis can reliably be made by 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid (99m-Tc DPD) scintigraphy without the need for histology.[3] Similar recommendations from American and Japanese authors are given in recently published review articles.[5,6] Accumulation of the radiotracer, however, may also be due to other myocardial changes, as illustrated by the following case.

Case report

A 68-year-old Caucasian male patient with a 13 year history of well-controlled arterial hypertension had been hospitalized in a tertiary medical centre with an acute ST-elevation myocardial infarction of the anterior wall. He had not suffered from angina pectoris before the acute event. Emergency coronary angiography showed a one-vessel disease. The

proximally occluded left anterior descending coronary artery (LAD) was recanalized, and two drug-eluting stents were implanted. Peak creatine kinase (5.385 U/L) and troponin T (8.835 ng/L) occurred 11 h after onset of symptoms and 8 h after recanalization.

One day after the coronary intervention, transthoracic echocardiography showed a left ventricle of normal size with hypokinesia of the apical and midventricular anterior wall, apical and midventricular interventricular septum as well as inferoapical and apicoposterolateral regions. The left atrium was slightly enlarged; the right atrium was normally sized. Left ventricular systolic function was on the lower limit of normal. The left ventricular myocardium was thickened (14 mm) with a 'granular sparkling' appearance of the myocardial texture (*Figure 1A*). The mitral and aortic valves were slightly thickened and showed an aortic and mitral regurgitation grade 1. Doppler echocardiography revealed diastolic dysfunction with an E/e' ratio of 12.

Cardiac amyloidosis had been suspected because of the thickened myocardium, and the patient was investigated by 99m-Tc DPD whole-body bone scan 4 days after the coronary intervention.

Scintigraphy showed increased tracer uptake within the myocardium, which was classified as Perugini Score 2 (*Figure 2A*). Because monoclonal gammopathy was excluded by negative serum and urine immune fixation, the diagnosis of cardiac TTR amyloidosis had been established. The patient was discharged with a pharmacotherapy comprising acetylsalicylic acid, prasugrel, pantoprazole, atorvastatin, bisoprolol, valsartan, and spironolactone. A medication with tafamidis had been recommended, but the patient decided to seek for a second opinion in our institution.

Three months after the myocardial infarction, the patient was in heart failure New York Heart Association stage II. Bone scintigraphy was repeated using 99m-Tc-hydroxydiphosphate (99m-Tc-HDP) and showed no myocardial tracer uptake at all (*Figure 2B*). Six months after myocardial infarction, transthoracic echocardiography showed a left ventricular ejection fraction of 45–50% and hypokinesia of the midventricular and apical parts of the interventricular septum and anterior wall. The interventricular septum was 8 mm in thickness (*Figure 1B*). Cardiac magnetic resonance imaging revealed subendocardial and mid-myocardial late gadolinium enhancement within the supply area of the LAD (*Figure 3*). Genetic testing showed no mutation of the *TTR* gene. Based on these findings, the diagnosis of TTR amyloidosis was definitely excluded, and the patient was advised to abstain from the suggested medication with tafamidis.

Discussion

Most probably, myocardial oedema due to reperfusion injury was the cause for the transient left ventricular wall thickening and 99m-Tc DPD tracer uptake resulting in the erroneous diagnosis of cardiac TTR amyloidosis.

Coronary artery ischaemia–reperfusion results in myocardial oedema, with consequent myocyte swelling and myofibrillar and extracellular oedema.[7] Animal experiments have shown that myocardial oedema manifests echocardiographically as transient wall thickening, starting immediately after coronary reperfusion.[8]

In animal studies, an increased uptake of technetium-99m phosphorus radiopharmaceuticals (99mTc-P) in acute myocardial infarction has been described.[9] This phenomenon in ischaemic myocardium is explained by selective adsorption of 99mTc-P from tissue calcium stores, including amorphous calcium phosphate, crystalline hydroxyapatite, and calcium complexed with myofibrils and other macromolecules, possibly supplemented by calcium-independent complexing with organic macromolecules.[9] In animals with experimentally

Figure 1 Transthoracic echocardiography (apical four-chamber view) 1 day after myocardial infarction shows a thickened interventricular septum (IVS = 14 mm) with an echogenic texture of the myocardium (A). Seven months after myocardial infarction, the diameter of the walls and the interventricular septum are within the normal range (IVS = 8 mm) (B).

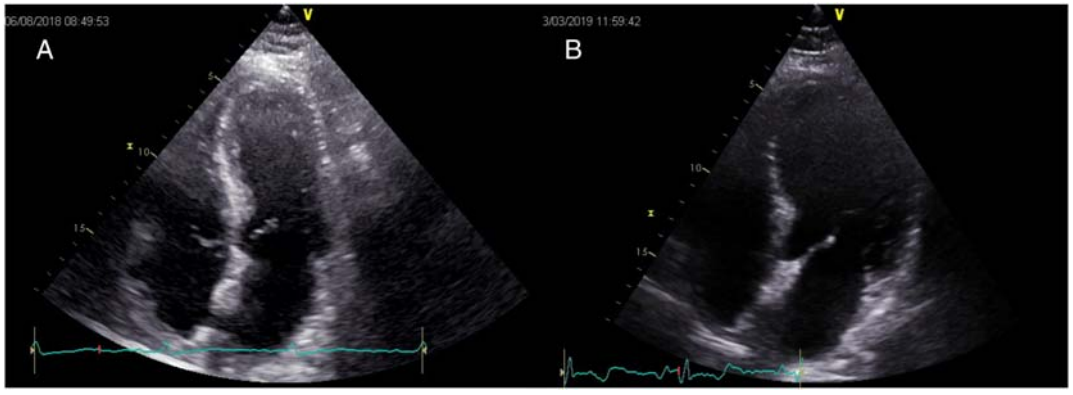
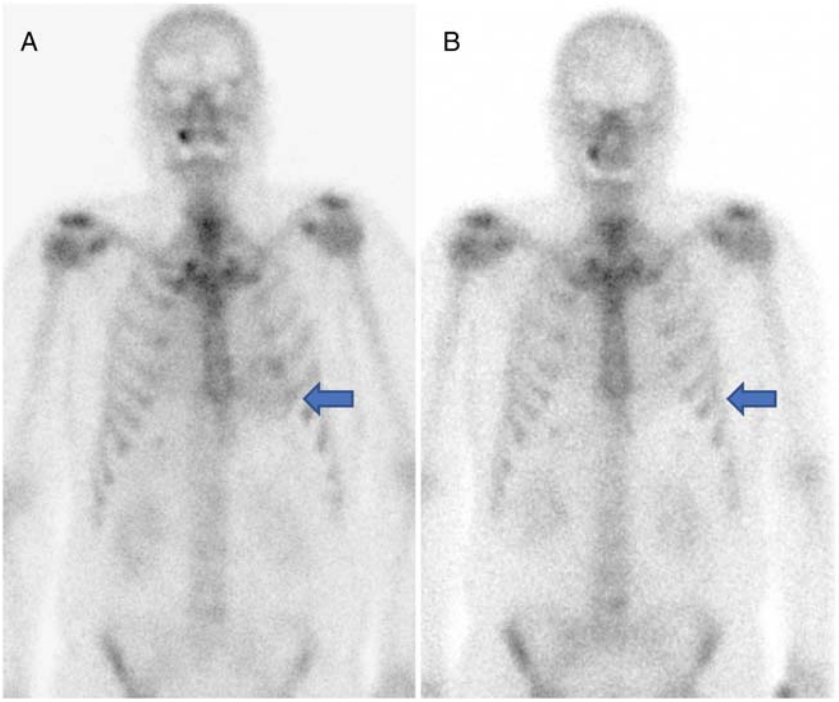


Figure 2 99m-Tc DPD/HDP bone scintigraphy 4 days after myocardial infarction shows a myocardial tracer uptake Perugini Score 2 (blue arrow) (A). Three months after myocardial infarction, scintigraphy does not show any cardiac uptake of technetium (B).



induced myocardial infarction, the tracer uptake was higher after coronary reperfusion than in animals with permanent coronary occlusion.[10] After coronary reperfusion, morphologic investigation showed oedema, congestion, haemorrhage, and damaged myocardiocytes.[10]

Also in humans, a positive scintigraphy with 99mTc-P was found within the first 6 days after myocardial infarction.[11] Follow-up scintigraphy in these patients, 17 to 20 days after myocardial infarction, showed decreased activity except for one patient, who developed pericarditis and a pulmonary embolus. Eight patients, in whom myocardial infarction was ruled out, showed no technetium uptake 1 to 5 days after onset of chest pain. Two patients with confirmed myocardial infarction showed no technetium uptake, as the scintigraphy was performed only 10–12 days after myocardial infarction. From these findings, the authors concluded that 99m-Tc DPD scintigraphy is highly positive in humans 1 to 6 days after myocardial infarction, then fades and usually disappears after 14 days.[11]

The described phenomenon, that not only cardiac TTR amyloidosis but also acute myocardial infarction, especially after reperfusion, may lead to positive technetium-99m phosphorus scans, is only sporadically mentioned in recent review articles.[4,12] To differentiate between amyloidosis and myocardial infarction, it is suggested to obtain information whether the uptake is regional—typical for ischaemia—or diffuse—typical for TTR amyloidosis.[4,12] In the presented patient, however, only projections in the anterior/posterior view had been performed; thus, no information about the regional tracer distribution is available.

The scintigraphic studies were performed with two different radiotracers: the initial investigation with technetium-99m diphosphono-propano-dicarboxylic acid and the follow-up investigation with technetium-99m hydroxymethylenediphosphonate. There are no indications from the literature that the different compounds used may explain the diverging results.[13]

When suspecting amyloidosis, not only echocardiographic findings but also history and clinical findings have to be considered. Except for myocardial thickening with granular sparkling by transthoracic echocardiography, the patient did not show any signs or symptoms suggesting TTR amyloidosis like a history of heart failure, arrhythmias, cardiac conduction system disease, carpal tunnel syndrome, lumbar spinal stenosis, biceps tendon rupture, or peripheral or autonomic neuropathy.[5,6] Granular sparkling is an echocardiographic finding that is not specific for amyloidosis but has also been reported in end-stage renal disease, hypertrophic cardiomyopathy, and Friedreich cardiomyopathy.[4,14,15] Myocardial thickening, furthermore, may be due to many different conditions and diseases.[15,16] In the case presented, inappropriate testing and interpretation of the images resulted in an

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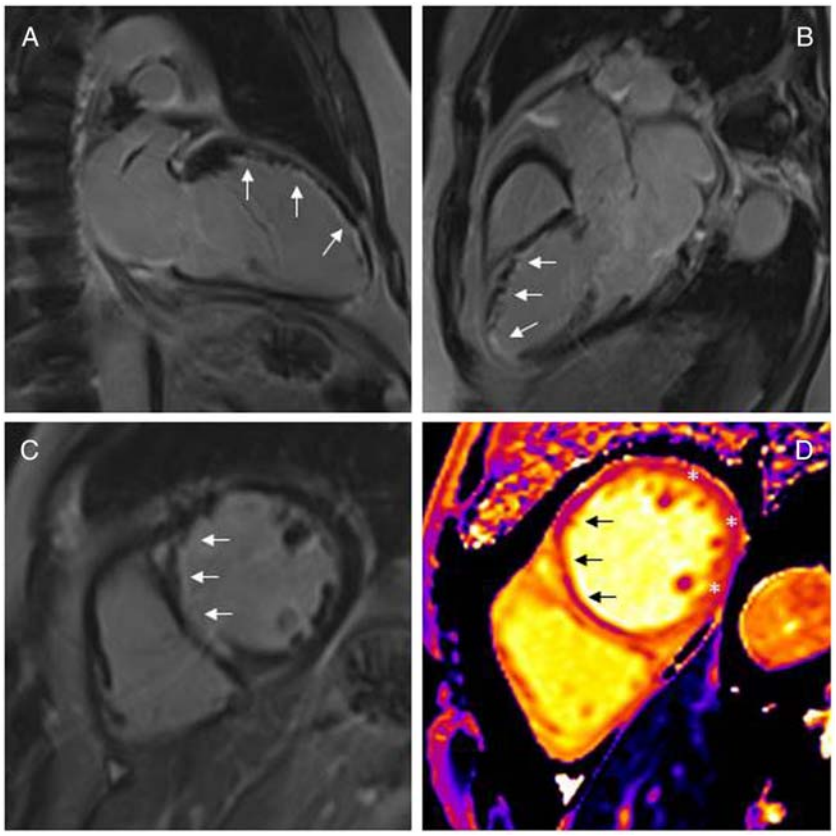
Figure 3 Cardiac magnetic resonance imaging (3 Tesla) 6 months after myocardial infarction shows subendocardial late gadolinium enhancement in the left anterior descending coronary artery in two-chamber (A) and three-chamber (B) as well as basal short axis view (C, white arrows). Compared with our healthy reference cohort (1194 ms average), anteroseptal (1220 ms, black arrows) and inferior/lateral (1160 ms) native T1 mapping (D) remains within the normal range.



erroneous diagnosis of cardiac TTR amyloidosis leading to distress for the patient and additional unnecessary diagnostic procedures.

At present, it is unknown how often cardiac TTR amyloidosis is erroneously diagnosed because physicians rely exclusively on echocardiographic and scintigraphic findings. Myocardial oedema with cardiac uptake of bone-avid radiotracers due to reperfused myocardial infarction is missing in current consensus papers, diagnostic algorithms, and state-of-the art reviews[1,3,5,6] and should be acknowledged as a differential diagnosis for cardiac TTR amyloidosis. In addition, a recent report demonstrated diffuse myocardial uptake of technetium-99m pyrophosphate in a patient with hydroxychloroquine-induced restrictive cardiomyopathy.[17]

Conclusions

From our case and the data presented, we conclude that myocardial oedema with cardiac uptake of bone-avid radiotracers due to reperfused myocardial infarction should be acknowledged as a differential diagnosis of cardiac TTR amyloidosis. The suspicion of cardiac amyloidosis should not be based on echocardiography and bone scintigraphy only but also on the history and clinical findings. When investigating patients with suspected cardiac TTR amyloidosis by scintigraphy, it has to be assessed if they have suffered from a recent myocardial infarction. Both planar and SPECT imaging should be performed in order to differentiate between diffuse and regional tracer uptake.

Conflict of interest

None declared.

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